Temperature Regulation
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SENSIBLE HEAT LOSS AFTER SYSTEMIC ANTICHOLINERGIC TREATMENT

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Summary

Systemic atropine administration decreases eccrine sweat gland release via competitive inhibition at cholinergic receptors and augments skin blood flow by a yet unknown mechanism. Increased skin blood flow promotes auxiliary radiative and convective heat flux by 20-100% in both warm and cold environments. These studies showed that the systemic dose of atropine (2 mg, im) was sufficient to block cholinergic sweat gland activity and core and skin temperatures were higher after atropine compared to control experiments. There was an enhanced skin blood flow thermosensitivity to esophageal temperature drive following atropine administration.

Introduction

Atropine or atropine-like antimuscarinic drugs block the action of acetylcholine at post-ganglionic cholinergic nerves, neuronal and ganglionic muscarinic receptors and smooth muscle cells that lack cholinergic innervation [1]. The most common cardiovascular effect of antimuscarinic drugs is an increased heart rate via blocking vagal stimulation of M_2 muscarinic receptors [1]. Since most vascular beds lack significant cholinergic innervation, the effects on blood vessels and blood pressure are not readily apparent [1]. However, during exercise in either hot or cold environmental conditions, systemic atropine administration dilates cutaneous vessels by a yet unknown mechanism which may be a compensatory vasodilator response to offset the rise in body temperature, or may be unrelated to cholinergic blockade [1]. This increase in skin blood flow after system atropine administration [2] increases radiative and convective heat flux in subjects whose skin temperature is warmer than the environment, and decreases heat gain in subjects whose skin temperature is lower than the ambient temperature. The increase in skin blood flow seen after atropine injection is greater than that occurring after the release of vasoconstrictor activity [3], and occurs even in cooler environments where the mean weighted skin temperature (as well as the local skin temperature) is below 33°C.

Materials and Methods

The effects of anticholinergic therapy, in this case intramuscular atropine sulfate (2 mg), on dry (sensible) and wet (insensible) heat exchange was studied in 22 healthy, young men in a series of studies. Their average (±SD) age was 21±3 yr; mass, 77.9±8.6 kg; surface area, 1.98±0.12 m^2; height 1.80±0.07 cm; body fat, 15.0±3.7%; and maximal aerobic power, 3.79±0.38 $L \cdot min^{-1}$. Experiments were done across a range of environmental conditions with dry bulb temperatures from 22 to 48°C and dew point temperatures from 7 to 24°C. Exercise intensity ranged from 30 to 55% of the measured maximal or peak aerobic power ($\dot{V}O_2$). All subjects were made familiar with all aspects of the testing and measurement procedures before data collection began. Subjects were tested once after the intramuscular injection of atropine sulfate (0.025 $mg \cdot kg^{-1}$; Elkin-Sinn, Cherry Hill, NJ, USA) and once after the injection of an equal volume of sterile saline. Test days were separated by a minimum of 48 h, and the order of drug presentation was counterbalanced. All experiments were single-blind.

Insensible, or *wet* heat exchange was calculated using partitional calorimetry as: $E_{sk} = M - (\pm W_k) - (R + C + K)$, in $W \cdot m^{-2}$. Specifically, evaporative heat loss from the skin surface was calculated as: $E_{sk} = (g \cdot min^{-1})(0.68\ W \cdot h \cdot g^{-1})(60\ min) \cdot m^{-2}$ in $W \cdot m^{-2}$. The maximal evaporative power of the environment was calculated as: $E_{max} = h_e(P_{s,sk} - P_{s,dp})$ in $W \cdot m^{-2}$. Whole body skin wettedness (w) was calculated from the ratio of E_{sk} to E_{max}. *Sensible* or *dry* heat exchange was calculated from the heat balance as: $(R+C) = M - (\pm W_k) \pm K - S$, in $W \cdot m^{-2}$. Specifically, radiative and convective heat exchange (R+C) was determined as: $R + C = (h_r + h_c)(T_s - T_a)$, in $W \cdot m^{-2}$.

Results and Discussion

The expected decrease in evaporative heat loss from the skin (E_{sk}) after atropine administration occurred in all environmental and exercise combinations and averaged -50%. This decrease in sweat secretion and evaporation due to antimuscarinic blockade at the sweat glands, decreased calculated whole body skin wettedness (w) an average of -60%. In contrast to the effect seen on insensible or wet heat loss, radiative and convective heat loss (sensible heat flux) increased after atropine treatment in all conditions studied. This increase ranged from 20 to 100% (20-40

$W \cdot m^{-2}$) depending on the specific conditions of the individual experiment. These results are summarized in Table 1.

Table 1. Insensible and sensible heat loss in multiple environments.

	CONTROL			ATROPINE		
T_a/P_w	E_{sk}	R+C	w	E_{sk}	R+C	w
22°C/0.8kPa	198	96	.56	84	113	.21
30°C/1.0kPa	234	32	.62	83	50	.19
42°C/1.6kPa	257	-85[a]	.72	139	-43	.29
48°C/2.4kPa	187	-150	.52	86	-116	.28
30°C/3.0kPa	145	27	.88	74	53	.27

[a]negative value indicates heat gain

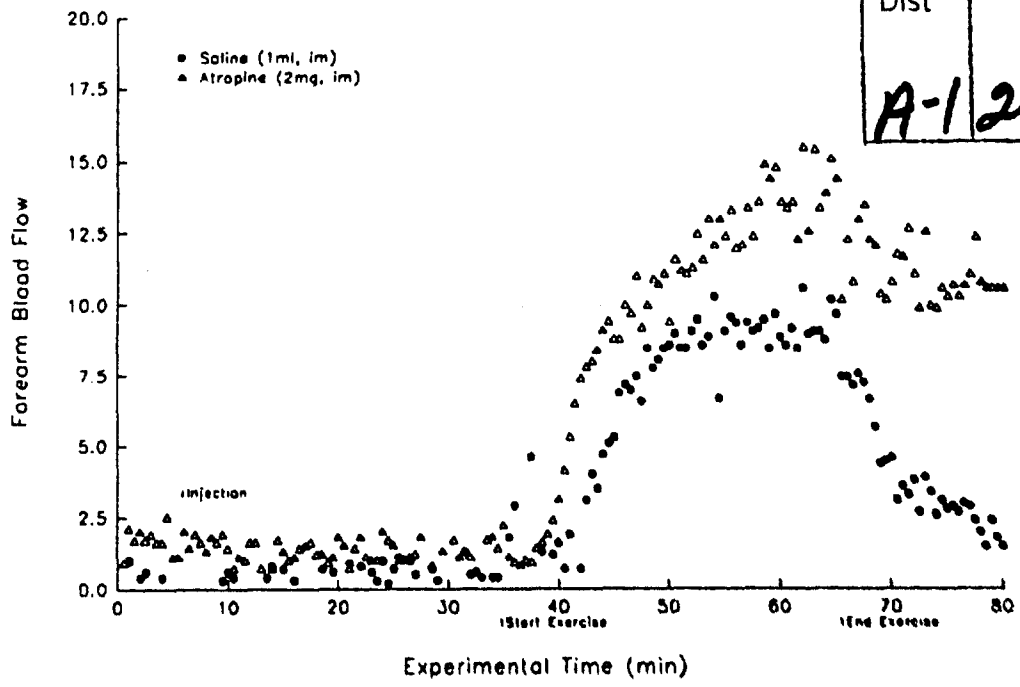

Figure 1. Forearm blood flow ($ml \cdot 100ml^{-1} \cdot min^{-1}$) during saline (control) and atropine experiments for a single subject.

In these studies, the systemic dose of atropine was sufficient to block cholinergic sweat gland activity and increase heart rate (~40 b•min^{-1}) during exercise compared to control experiments. Reports of enhanced cutaneous vasodilation, whether measured directly or calculated from the heat balance, were confirmed by these studies. An example of increased skin blood flow during exercise after the systemic administration of atropine sulfate is shown in Figure 1. In this example (T_a = 30°C, 55% peak $\dot{V}O_2$) atropine or a saline placebo was injected at 5 min and exercise began 30 min after the injection and ended at 65 min. Skin blood flow was 60% higher during exercise after atropine treatment. Both esophageal and mean weighted skin temperature were higher by the end of exercise but not at the time of increased skin blood flow after atropine treatment compared to saline. The data from Figure 1 are presented in Figure 2 as the forearm blood flow plotted against the esophageal temperature. These data indicate the slope of this relationship is increased with atropine treatment.

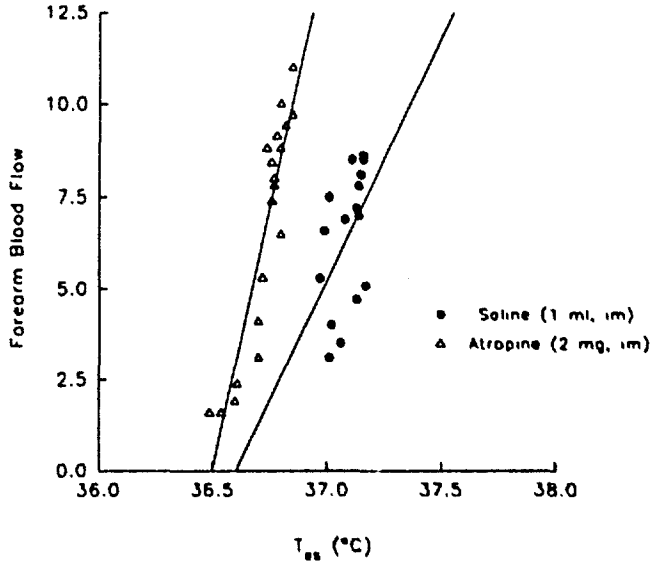

Figure 2. Forearm blood flow (ml•100ml^{-1}•min^{-1}) plotted against esophageal temperature during saline (control) and atropine experiments for a single subject. Note the increased thermosensitivity in the atropine experiment [4].

The observed changes in sensible and insensible heat loss after systemic atropine treatment are in opposite directions, although the increase in dry heat flux does not fully compensate for the decrease in evaporative heat loss. The mechanism(s) responsible for increased skin blood flow during exercise after systemic atropine treatment may include: 1) slightly higher local skin temperature [3], although this appears to be a passive function of the increased skin blood flow; 2) changing baroreflex activity [1,3,5,6], although cardiac output and mean arterial pressure are unchanged; 3) release of sympathetic vasoconstrictor activity [1,3,5], although increases in skin blood flow would be smaller than we observed; 4) the increase in skin blood flow, if neurogenic in nature, is non-cholinergic; 5) the chronotropic effect on the heart such that pulsatile flow or increase shear stress is transduced at the endothelium to increase endothelium-derived relaxing factors [7,8], such as nitric oxide; 6) the presence of other vasodilatory substances, perhaps related to the sweat gland [9]; or 7) a combination of any of the above.

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